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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/449,204	11/24/1999	ANTHONY H. DODGE	P1543R1	6001

7590 07/09/2002

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EXAMINER	
FORMAN, BETTY J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/449,204	DODGE ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,5,8-14,17-20 and 23-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,5,8-14,17-20 and 23-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 14 September 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/449,204 is acceptable and a CPA has been established. An action on the CPA follows.

2. This action is in response to papers filed 1 April 2002 in Paper No. 21 in which claims 17 and 23 were amended, claim 16 was canceled and claims 24-46 were added. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 14 dated 14 March 2001 are withdrawn in view of the amendments and new grounds for rejection. New grounds for rejection are discussed.

Currently claims 2, 4, 5, 8-14, 17-20 and 23-46 are under prosecution.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 2, 4, 5, 8-14, 17-20 and 23-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hendrickson et al. (Nucleic Acids Research, 1995, 23(3): 522-529) in view of

Gibson et al. (Genome Methods 1996, 6: 995-1001) and Gold et al. (U.S. Patent No. 5,475,096, filed 10 June 1991).

Regarding Claim 23, Hendrickson et al. teach a method for quantitating or detecting the presence of a target compound in a sample, the method comprising: exposing the sample to a capture molecule which binds to the target molecule to form a capture molecule-target molecule complex, adding to the complex a nucleic acid moiety containing a detector molecule wherein the detector molecule binds to the target molecule to form a capture molecule-target molecule-detector molecule complex, amplifying the nucleic acid moiety by PCR amplification, and quantitating or detecting the PCR amplified nucleic acid moiety (page 523, Fig. 1) the target molecule is present at a concentration equal to or less than about 5000 pg/mL (page 526, right column, first full paragraph and Fig. 4). Hendrickson et al. do not teach the method wherein the detector molecule is an RNA aptamer and the amplified RNA is quantitated or detected using a detectable non-primer probe and real-time PCR. However, aptamers were well known in the art and used to detect as taught by Gold et al. (Column 8, lines 22-45) and real-time PCR using detectable non-primer probes was also well known and routinely practiced in the art at the time the claimed invention was made as taught by Gibson et al. Specifically, Gibson et al. teach a method for detecting a PCR amplified product with sequence-specific non-primer probes using real-time PCR (page 997, right column, page 1000, last paragraph and Table 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the detection of Hendrickson et al. wherein aliquots of the PCR reaction are run on agarose gel for detection and quantitation of amplified product at a single time point (page 525, right column, second full paragraph) with the Gibson et al. method wherein the PCR reaction is detected and quantitated every 8.5 seconds (page 996, left column, lines 1-3) by detection of non-primer probe hybridization for the expected benefit of eliminating the agarose gel step and for the expected benefit of accurate and time-saving detection as taught by Gibson et al. (page 995, right column, lines 1-5). Additionally, Gold et al. teach that

aptamers can be employed as antibodies have conventionally been employed in detection assays and they teach aptamers have numerous advantages over antibodies i.e. aptamers can be readily amplified, they do not require animal immunization and the binding affinity of aptamers can be tailored to users needs (Column 8, lines 37-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the antibody-detector molecule of Hendrickson et al. with the aptamer-detector molecule of Gold et al. for the expected benefit of specific, qualitative and quantitative detection of target molecules as taught by Gold et al. (Column 27, lines 54-56) and for the additional benefits of aptamers i.e. aptamers can be readily amplified, they do not require animal immunization and the binding affinity of aptamers can be tailored to used needs as taught by Gold et al. (Column 8, lines 37-45).

Regarding Claim 2, Hendrickson et al. teach the method further comprising washing the capture molecule-target molecule complex to remove unbound sample after step (a) (page 525, left column, third full paragraph, lines 5-6).

Regarding Claim 4, Hendrickson et al. teach the method wherein the capture molecule is bound to a solid support (page 1372, Fig. 1).

Regarding Claim 5, Hendrickson et al. teach the method wherein the capture molecule is bound to a solid support (page 1372, Fig. 1) but they do not teach the method wherein the capture molecule is in solution during step (a) or (b). However, binding of capture molecule-target molecules in solution was routinely practiced in the art. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the immobilized capture of Hendrickson et al. with capture molecules in solution for the known benefit of binding capture-to-target molecules in large volumes for the obvious benefit of more rapid binding in solution as known in the art.

Regarding Claim 8, Hendrickson et al. teach the method wherein the target molecule is an organic compound having a molecular weight of about 100 to about 1000 grams/mole i.e.

human thyroid stimulating hormone (hTSH) (page 523, left column, second full paragraph, lines 1-3).

Regarding Claim 9, Hendrickson et al. teach the method of wherein the target molecule is a protein i.e. hTSH (page 523, left column, second full paragraph, lines 1-3).

Regarding Claim 10, Hendrickson et al. teach the method of wherein the target molecule is a protein i.e. hTSH (page 523, left column, second full paragraph, lines 1-3).

Regarding Claim 11, Hendrickson et al. do not teach the method wherein the sample is selected from the group consisting of blood, serum, sputum, urine, semen, cerebrospinal fluid, bronchial aspirate and organ tissue. However, Hendrickson et al. teach the method detects hTSH known to be present in blood (page 526, left column, last paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the method for detecting hTSH is a sample as taught by Hendrickson et al. to samples known to contain hTHS for the expected benefit of highly sensitive detection of hTSH (a clinically important target molecule) in blood as taught by Hendrickson et al. (page 528, last paragraph).

Regarding Claim 12, Hendrickson teach the method wherein the capture molecule is immobilized on a solid support (page 525, left column, second full paragraph, lines 1-6) but they do not teach the immobilization is via biotin labeled capture molecule bound to a streptavidin or avidin labeled support. However, biotin-labeled capture molecules immobilized via binding to a streptavidin or avidin labeled support were known and routinely practiced in the art at the time the claimed invention was made. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the immobilization of Hendrickson et al. with routinely practiced biotin-avidin immobilization for the known benefit of rapid and specific biotin-avidin immobilization.

Regarding Claims 13-14, Hendrickson et al. do not teach quantitation or detection using a non-primer probe having a fluorescent dye label (Claim 13) wherein the fluorescent dye label comprises two dyes (Claim 14). However, Gibson et al. teach quantitation of the amplified

nucleic acid moiety using a detectable non-primer probe having a fluorescent dye label (page 996, right column lines 1-4) wherein the fluorescent dye label comprises two dyes, a reporter dye and a quencher dye which fluoresce at different wavelengths (page 996, right column lines 1-16). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the detection of Hendrickson et al. with the two-dye fluorescent detection of Gibson et al. wherein fluorescently labeled non-primer probes are detected to quantitate PCR product by monitoring fluorescence emission and quenching (page 996, right column, lines 1-16) for the obvious benefit of detecting and quantitating amplified product over an extended period of time and for the expected benefit of accurate and time-saving detection as taught by Gibson et al. (page 995, right column, lines 1-5).

Regarding Claims 17-19, Hendrickson et al. do not teach the detector molecule is RNA and the RNA is reverse transcribed to form DNA before or during amplifying (Claim 17), at a temperature sufficient to dissociate the detector molecule (Claim 18) and at a temperature about 50 to about 70°C (Claim 19). However, Gold et al. teach aptamers are RNA (Column 14, lines 34-35) which are reverse transcribed before amplifying (Column 13, lines 39-51). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the DNA of Hendrickson et al. with RNA as taught by Gold et al. based on target to be detected and desired results and to reverse transcribed the RNA to DNA before amplification as taught by Gold et al. and for the expected benefits of amplification using the polymerase chain reaction (Gold et al., Column 13, lines 40-42). Additionally, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to reverse transcribe the RNA detector molecule at a temperature sufficient to dissociate the detector molecule and specifically between 50 and 70°C for the obvious benefit of transcribing the RNA at temperature which prevents secondary structure of the RNA and for the expected benefit of partitioning the RNA detector molecule for identification as taught by Gold et al. (Column 1, lines 14-31).

Regarding Claim 20, Hendrickson et al. teach the method wherein the solid support is a 96-well thermowell microtitre plate which is placed into a thermal cycler for PCR amplification (page 525, left column, second full paragraph, lines 1-4 and fourth paragraph, lines 1-3) but they do not teach the solid support is a PCR tube. However, 96-well microtitre plates and PCR tubes were known and routinely practiced in the art for one-well/sample and one-tube/sample wherein reagent mixing and nucleic acid amplification for each sample is in isolation. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the 96-wells PCR solid support of Hendrickson et al. with a single-well PCR solid support based the number of samples to be assayed, available equipment and experimental design for the obvious benefit of reducing the cost and labor involved with 96-format assays by performing single-format assays.

Regarding Claims 24-45, Hendrickson et al. teach the method wherein the target molecule is quantitated at a concentration equal to or less than 1 pg/mL (Claims 14-16) about 100 to about 5000 pg/ml (Claims 27-29); of about 3 to 100 pg/ml (Claims 30-32); of about 0.4 to about 100pg/ml (Claims 33-35); of about 1 to about 100 pg/ml (Claims 36-38); of about 0.03 of about 100 pg/ml (Claims 39-41); of about 0.005 to about 1 pg/ml (Claims 42-44) (page 526, right column, first full paragraph and Fig. 4).

Regarding Claim 46, Hendrickson et al. teach a method for quantitating or detecting the presence of a target compound in a sample, the method comprising: exposing the sample to a capture molecule which binds to the target molecule to form a capture molecule-target molecule complex, adding to the complex a nucleic acid moiety containing a detector molecule wherein the detector molecule binds to the target molecule to form a capture molecule-target molecule-detector molecule complex, amplifying the nucleic acid moiety by PCR amplification, and quantitating or detecting the PCR amplified nucleic acid moiety (page 523, Fig. 1). Hendrickson et al. do not teach the method wherein the detector molecule is an RNA aptamer and the amplified RNA is quantitated or detected using a detectable non-primer probe and real-

time PCR. However, aptamers were well known in the art and used to detect as taught by Gold et al. (Column 8, lines 22-45) and real-time PCR using detectable non-primer probes was also well known and routinely practiced in the art at the time the claimed invention was made as taught by Gibson et al. Specifically, Gibson et al. teach a method for detecting a PCR amplified product with sequence-specific non-primer probes using real-time PCR (page 997, right column, page 1000, last paragraph and Table 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the detection of Hendrickson et al. wherein aliquots of the PCR reaction are run on agarose gel for detection and quantitation of amplified product at a single time point (page 525, right column, second full paragraph) with the Gibson et al. method wherein the PCR reaction is detected and quantitated every 8.5 seconds (page 996, left column, lines 1-3) by detection of non-primer probe hybridization for the expected benefit of eliminating the agarose gel step and for the expected benefit of accurate and time-saving detection as taught by Gibson et al. (page 995, right column, lines 1-5). Additionally, Gold et al. teach that aptamers can be employed as antibodies have conventionally been employed in detection assays and they teach aptamers have numerous advantages over antibodies i.e. aptamers can be readily amplified, they do not require animal immunization and the binding affinity of aptamers can be tailored to users needs (Column 8, lines 37-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the antibody-detector molecule of Hendrickson et al. with the aptamer-detector molecule of Gold et al. for the expected benefit of specific, qualitative and quantitative detection of target molecules as taught by Gold et al. (Column 27, lines 54-56) and for the additional benefits of aptamers i.e. aptamers can be readily amplified, they do not require animal immunization and the binding affinity of aptamers can be tailored to used needs as taught by Gold et al. (Column 8, lines 37-45).

5. Claims 2, 4, 5, 8-14, 17-20 and 23-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cubicciotti (U.S. Patent No. 6,287,765, filed 20 May 1998) in view of Hendrickson et al. (Nucleic Acids Research, 1995, 23(3): 522-529) and Gibson et al. (Genome Methods 1996, 6: 995-1001).

Regarding Claim 23, Cubiccoitti teaches a method for quantitating or detecting the presence of a target compound in a sample, the method comprising: exposing the sample to a capture molecule which binds to the target molecule to form a capture molecule-target molecule complex, adding to the complex a nucleic acid moiety containing a detector molecule wherein the detector molecule binds to the target molecule to form a capture molecule-target molecule-detector molecule complex, amplifying the nucleic acid moiety by PCR amplification, and quantitating or detecting the PCR amplified nucleic acid moiety (Column 229, lines 5-52) but they are silent regarding the concentration of the target molecule. However, detection of targets at a concentration of equal to or less than 5000 pg/ml was well known in the art at the time the claimed invention was made as taught by Hendrickson et al who teach a method similar to that of Cubiccoitti wherein the target is wherein the target molecule is present at a concentration of equal to or less than 5000 pg/mL (page 526, right column, first full paragraph and Fig. 4). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the well known detection sensitivity of Hendrickson et al to detect target molecules of 5000 pg/ml or less for the obvious benefits of detecting clinically important low-copy number targets. Cubiccoitti teaches that the aptamers are amplified and detected using well known techniques (Column 155, lines 26-50) but they do not specifically teach the detection is via real time PCR. However, real-time PCR using detectable non-primer probes was well known and routinely practiced in the art at the time the claimed invention was made as taught by Gibson et al. Specifically, Gibson et al. teach a method for detecting a PCR

amplified product with sequence-specific non-primer probes using real-time PCR (page 997, right column, page 1000, last paragraph and Table 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply real time PCR of Gibson et al to the detection of Cubiccoitti and to detect and quantitate PCR products every 8.5 seconds (page 996, left column, lines 1-3) by detection of non-primer probe hybridization for the expected benefit of eliminating the agarose gel step and for the expected benefit of accurate and time-saving detection as taught by Gibson et al. (page 995, right column, lines 1-5).

Regarding Claim 2, Cubicciotti teaches the method further comprising washing the capture antibody: target molecule complex to remove unbound sample i.e. affinity chromatography (Column 229, lines 26-32)

Regarding Claim 4, Cubicciotti teaches the method wherein the capture antibody is bound to a solid support during step a or b (Column 221, lines 19-42).

Regarding Claim 5, Cubicciotti teaches the method wherein the capture antibody is in solution during step a or b (Column 229, lines 15-26).

Regarding Claim 8, Cubicciotti teaches the method wherein the target molecule is an organic compound having a molecular weight of about 100 to about 1000 grams/mole i.e. therapeutic peptide 7E3 (Column 228, lines 20-30).

Regarding Claim 9, Cubicciotti teaches the method of wherein the target molecule is a protein i.e. therapeutic peptide 7E3 (Column 228, lines 20-30).

Regarding Claim 10, Cubicciotti teaches the method of wherein the target molecule is a cytokine as claimed (Column 31, lines 1-17).

Regarding Claim 11, Cubicciotti teach the method wherein the sample is selected from the group consisting of blood, serum, sputum, urine, semen, cerebrospinal fluid, bronchial aspirate and organ tissue (Column 229, lines 5-15).

Regarding Claim 12, Cubicciotti teaches the method wherein the capture molecule is immobilized on a solid support via biotin (Column 163, lines 5-21).

Regarding Claims 13-14, Cubicciotti does not teach quantitation or detection using a non-primer probe having a fluorescent dye label (Claim 13) wherein the fluorescent dye label comprises two dyes (Claim 14). However, Gibson et al. teach quantitation of the amplified nucleic acid moiety using a detectable non-primer probe having a fluorescent dye label (page 996, right column lines 1-4) wherein the fluorescent dye label comprises two dyes, a reporter dye and a quencher dye which fluoresce at different wavelengths (page 996, right column lines 1-16). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the detection of Cubicciotti with the two-dye fluorescent detection of Gibson et al. wherein fluorescently labeled non-primer probes are detected to quantitate PCR product by monitoring fluorescence emission and quenching (page 996, right column, lines 1-16) for the obvious benefit of detecting and quantitating amplified product over an extended period of time and for the expected benefit of accurate and time-saving detection as taught by Gibson et al. (page 995, right column, lines 1-5).

Regarding Claims 17-19, Cubicciotti teaches the method wherein the detector molecule is RNA and the RNA is reverse transcribed to form DNA before or during amplifying (Claim 17), at a temperatures well known in the art (Claims 18 & 19) (Column 153, line 33-Column 154, line 35). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply well known temperatures for reverse transcription and dissociation to the RNA detectors of Cubicciotti e.g. between 50 and 70°C for the obvious benefit of transcribing the RNA at temperature which prevents secondary structure of the RNA and for the expected benefit of partitioning the RNA detector molecule for identification.

Regarding Claim 20, Cubicciotti teaches the method wherein the solid support is a 96-well microtitre plate (Column 229, lines 15-26) but they do not specifically teach the 96-well plate is a PCR microtiter plate. However, 96-well microtitre plates and PCR tubes were known and routinely practiced in the art for one-well/sample and one-tube/sample wherein reagent mixing and nucleic acid amplification for each sample is in isolation. It would have been

obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the 96-wells PCR solid support of Hendrickson et al. with a single-well PCR solid support based the number of samples to be assayed, available equipment and experimental design for the obvious benefit of reducing the cost and labor involved with 96-format assays by performing single-format assays.

Regarding Claims 24-45, Cubicciotti is silent regarding the concentration of the target molecule. However, detection of targets at a concentration of equal to or less than 5000 pg/ml was well known in the art at the time the claimed invention was made as taught by Hendrickson et al who teach a method similar to that of Cubiccoitti wherein the target is wherein the target molecule is present at a concentration of equal to or less than 5000 pg/mL (page 526, right column, first full paragraph and Fig. 4). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the well known detection sensitivity of Hendrickson et al to detect target molecules at a concentration equal to or less than 1 pg/mL (Claims 14-16) about 100 to about 5000 pg/ml (Claims 27-29); of about 3 to 100 pg/ml (Claims 30-32); of about 0.4 to about 100pg/ml (Claims 33-35); of about 1 to about 100 pg/ml (Claims 36-38); of about 0.03 of about 100 pg/ml (Claims 39-41); of about 0.005 to about 1 pg/ml (Claims 42-44) as taught by Hendrickson et al (page 526, right column, first full paragraph and Fig. 4) of 5000 pg/ml or less for the obvious benefits of detecting clinically important low-copy number targets.

6. Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cubicciotti (U.S. Patent No. 6,287,765, filed 20 May 1998) in view of Gibson et al. (Genome Methods 1996, 6: 995-1001).

Regarding Claim 46, Cubiccoitti teaches a method for quantitating or detecting the presence of a target compound in a sample, the method comprising: exposing the sample to a capture molecule which binds to the target molecule to form a capture molecule-target molecule complex, adding to the complex a nucleic acid moiety containing a detector molecule wherein the detector molecule binds to the target molecule to form a capture molecule-target molecule-detector molecule complex, amplifying the nucleic acid moiety by PCR amplification, and quantitating or detecting the PCR amplified nucleic acid moiety (Column 229, lines 5-52). Cubiccoitti teaches that the aptamers are amplified and detected using well known techniques (Column 155, lines 26-50) but they do not specifically teach the detection is via real time PCR. However, real-time PCR using detectable non-primer probes was well known and routinely practiced in the art at the time the claimed invention was made as taught by Gibson et al. Specifically, Gibson et al. teach a method for detecting a PCR amplified product with sequence-specific non-primer probes using real-time PCR (page 997, right column, page 1000, last paragraph and Table 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply real time PCR of Gibson et al to the detection of Cubiccoitti and to detect and quantitate PCR products every 8.5 seconds (page 996, left column, lines 1-3) by detection of non-primer probe hybridization for the expected benefit of eliminating the agarose gel step and for the expected benefit of accurate and time-saving detection as taught by Gibson et al. (page 995, right column, lines 1-5).

Conclusion

7. No claim is allowed.

8. The examiner's Art Unit has changed from 1655 to 1634. Please address future correspondence to Art Unit 1634.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
July 1, 2002